REMARKS:

Careful consideration has been given to the Official Action of June 26, 2003 and reconsideration of the application as amended is respectfully requested.

The abstract has been amended to correct a typo that was pointed out by the Examiner.

The Examiner has objected to the claim section for not having an appropriate introductory phrase. The claim section has been amended to begin with the phrase "We claim:" to overcome the Examiner's objection.

The Examiner has rejected claims 20-42 under 35 U.S.C. § 112 first paragraph as failing to comply with the written description requirement. Claims 21, 30, 32, 35, and 36 are rejected under 35 U.S.C. § 112 second paragraph as being indefinite.

Claims 20, 22-26, 28-39, and 41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. (U.S. Pat. No. 6,141,582) in view of Hofmann (U.S. Pat. No. 6,208,893). Claim 21 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. in view of Hofmann and further in view of Gough et al. (U.S. Pat. No. 5,928,229). Claim 27 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. in view of Hofmann and further in view of Eggers et al. (U.S. Pat. No. 5,928,159). Claim 40 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Mori et al. in view of Hofmann and further in view of Mawad (U.S. Pat. No. 6,428,462).

In order to overcome the rejections noted above, claims 20-41 have been canceled and new claims 42-75 have been added The new claims are fully supported by the specification and the drawing figures. Thus no new matter has been introduced. New independent claim 42 is a generic claim directed to the apparatus disclosed by the present

invention. New independent claims 70 and 71 are directed to the registration and conversion device and the method for implementing the apparatus respectively.

New claims 42-75 are clearly distinguishable from the prior art as discussed hereafter.

An essential distinguishing characteristic of the present invention is that a registration, conversion and evaluation device is provided to calculate, based on the impedance measurements, the amount of poration achieved after each electroporation pulse and then, from the calculated result, decides whether the desired amount of electroporation is reached. In order to do so, the device measures and stores the impedance values before the electroporation pulse and then, using mathematical algorithms, compares the previous measurements with the measurement taken after the electroporation pulse in order to assess the amount of electroporation that has occurred. By measuring the impedance prior to, during and after providing a pulse it is possible to detect and determine when the treatment is finalized.

In contrast with the present invention, Mori et al. discloses an iontophoresis system that is used to introduce medical substances and molecules into a living body through the skin. The technique is one among other possible ways to introduce medical substances into a patient. Examples of other methods of introduction are digestion, injection and inhalation.

The present invention is related to electroporation which is not used to introduce medical substance or molecules into the patient's body but to increase the uptake of substances into the cells. The substances have to be introduced into the body with, for example, one of the above mentioned methods, either before or after the high voltage pulses. Normally electroporation is combined with injection as the preferred method for introduction. The substances that are used in combination with electroporation usually have very little or

no effect when they are introduced into the body without the combination with electroporation. It is therefore mandatory to use electroporation or some other method for introduction into the cells for these substances to have the desired effect.

The iontophoresis system as described by Mori et al. uses low voltages (1-20V and preferably 3-12V) over long time periods. (Column 10, lines 3-13) Conversely, the present invention uses a high voltage generator (50-6000V) operating during shorter periods, for example, 32 pulses at 0.1-10 kHz. The present invention is also coupled to an impedance measuring unit which measures the impedance at one or more frequencies. On the other hand, the iontophoresis system measures the current at only one frequency. By measuring impedance at several frequencies, the apparatus is able to ensure that the electroporation is performed only during the time period necessary to enable the possibility of introducing molecules into the cells in the tissue or organ without either destroying the cells in the tissue or organ or influence the surrounding tissue or organs in the case a tumor is treated.

It is well documented that there is a minimum threshold voltage that must be present over the cell membrane in order for electroporation to occur. If the voltage is lower than the minimum threshold voltage, no electroporation will take place. In contrast, an iontophoresis system as disclosed by Mori et al. uses small electrical currents (0.01-10 mA/cm^2) to enhance the uptake of substances trough the skin. Low voltages such as the 20V maximum which is commonly used in an iontophoresis system is not able to cause any electroporation. However, voltages that are high enough to cause electroporation are not suitable in an iontophoresis system since the high voltages would cause pain that would be totally unacceptable for the treated patient-- it is a completely different system and a person skilled in the art would not start from such a system to develop a new apparatus which in a controlled way by the use of a

high voltage generator can electroporate cells in tissues or organs without destroying the cells in the tissue or organ. Additionally, for the treatment of tumors it is very important to eliminate the tumors without affecting the surrounding tissue or organ cells.

It should be noted that in an iontophoresis system as disclosed by Mori et al., the impedance measured during the treatment is not performed to assess if any electroporation occurs, but rather to measure completely different biological effects that the small currents and voltages have on the skin and mucosa layer and to adjust voltages and currents in order to control and maximize the transport of ionic medical compounds into the body.

The method provided by the present invention for assessing the cell poration during electroporation works in a very different way when compared to the cited art. The registration, conversion and evaluation device which calculates, based on the impedance measurements at different frequencies, the amount of poration achieved after each electroporation pulse and then, from the calculated result, decides whether the desired amount of electroporation is reached.

Secondary references applied by the Examiner are directed to features no longer claimed and are no longer relevant to the new claims which have been added.

Independent claims 42, 67 and 68 now recite that the impedance measuring unit is arranged between the plurality of electrodes to measure the impedance before, during and after application of the high voltage pulses at one or more frequencies, and find no such disclosure in the cited art.

On the basis of the above action and remarks, it is respectfully submitted that the application is in allowable condition and favorable reconsideration is earnestly solicited.

Respectfully submitted,

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